



NAVY DEPARTMENT

BUMED NEWS LETTER

a digest of timely information

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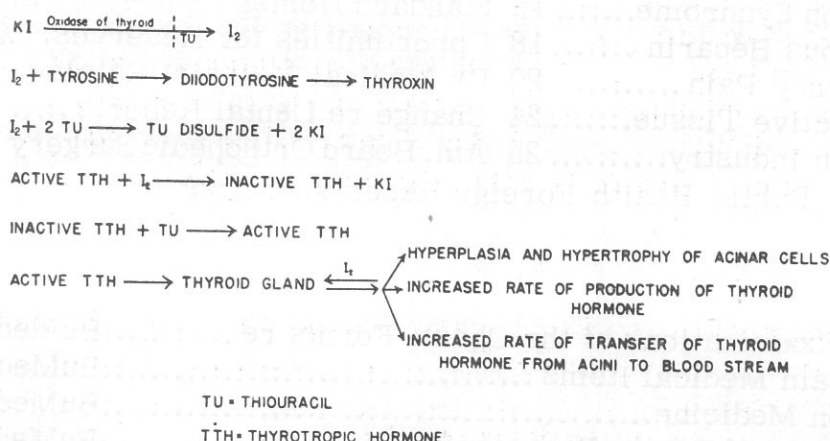
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Drugs and Surgery in Thyrotoxicosis: The obscurity of the fundamental disturbances in the body leading to the development of thyrotoxicosis has interfered with a direct approach in the therapy of this disease. Although progress has been made in controlling it by surgical measures, much is left to be desired, both as concerns the principles and the results of treatment. The ideal therapy is one which is simple, inexpensive, available to everyone, does not necessitate hospitalization, is not associated with significant toxic reactions and does not permit much invalidism. These ideals do not seem to be as reasonable an expectation with surgical treatment as with chemotherapy or physical therapy.

Recent contributions to the physiology of the thyroid have led to a clearer understanding of some of the problems of thyrotoxicosis. Whereas complete proof does not substantiate some of the hypotheses that have been advanced, they serve as logical working bases. The thyrotropic hormone tends to keep the thyroid gland active, the amount of stimulation varying in intensity with environmental changes.

PRESUMPTIVE BIOCHEMICAL REACTIONS IN THE THYROID GLAND



Sites of therapy for toxic diffuse goiter. It is not known definitely that all these reactions take place in the body, but at present it seems likely that they do. It can be noted that iodine is an extremely active compound when it is in elemental form and that some of its reactions, as well as those of thiouracil, are antagonistic to each other, as far as the picture of thyrotoxicosis is concerned; moreover, the two compounds are antagonistic to each other.

As is illustrated in the chart above, an excessive quantity of thyrotropin, as in toxic diffuse goiter, leads to (a) hyperplasia and hypertrophy of the acinar cells of the thyroid gland, (b) increased rate of production of thyroid hormone, and (c) increased rate of transfer of thyroid hormone from the acini to the blood. The thyroid hormone exists in the acini as thyroglobulin. Except at the time of thyroidectomy or possibly with destructive lesions of the thyroid gland, thyroglobulin apparently does not exist in the blood stream, because it is too large a molecule to enter the blood vessel. Proteolytic enzymes in the thyroid have been shown to break down the globulin portion of thyroglobulin, permitting absorption of the active material into the blood stream; iodine inhibits this proteolytic action. Indeed, iodine participates in many reactions

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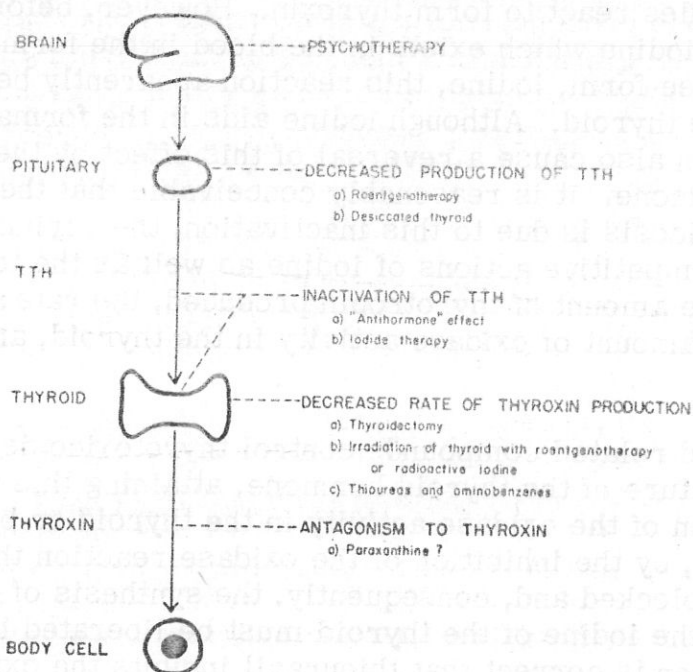
in the thyroid gland. It is added to tyrosine to form diiodotyrosine, and then two of these molecules react to form thyroxin. However, before iodination can take place, the iodine which exists in the blood in the form of iodide must be changed to its free form, iodine, this reaction apparently being produced by an oxidase in the thyroid. Although iodine aids in the formation of the thyroid hormone, it can also cause a reversal of this effect by the inactivation of the thyrotropic hormone. It is reasonably conceivable that the effect of iodide therapy in thyrotoxicosis is due to this inactivation, the variability in results depending on the competitive actions of iodine as well as the total amount of iodine available, the amount of thyrotropin produced, the rate of reactivation of thyrotropin, the amount of oxidase activity in the thyroid, and many other factors.

Thiouracils and related compounds control thyrotoxicosis by decreasing the rate of manufacture of the thyroid hormone, attaining this result, conceivably, by the inhibition of the oxidase activity in the thyroid or by reacting with iodine. Apparently, by the inhibition of the oxidase reaction the conversion of iodide to iodine is blocked and, consequently, the synthesis of diiodotyrosine is antagonized. If the iodine of the thyroid must be liberated by an oxidase, and if the assumption is correct that thiouracil inhibits the oxidase reaction, it would seem unnecessary to assume that the capacity of thiouracil to react with iodine plays a significant role in antithyrotoxicosis, because the iodine would remain in the form of iodide and, hence, would not react with thiouracil. Moreover, the amount of antithyroid action of the thiouracils is not proportional to the capacity of the compounds to react with iodine, forming thiouracil disulfide and an iodide. For example, 6-aminothiouracil and thiouracil react about equally with iodine, but the latter has a thousand times as much antithyroid action in rats.

The fact that thiouracil activates thyrotropic hormone may explain the increase in the size of the goiter and the increase in manifestations of malignant exophthalmos that occur in a few patients while they are still thyrotoxic.

There are a number of structures, especially the central nervous system, pituitary, and thyroid, as well as the body cells as a whole, that modify the rate of metabolism in the body, as shown in the chart on the following page. Moreover, these units exert a significant effect on one another, directly and indirectly. Consequently, it is not surprising to note that in the treatment of thyrotoxicosis attempts have been made to influence the function of these entities. Psychotherapy alone is successful in some cases. Roentgenotherapy applied to the pituitary has been claimed to be of some success. In a small proportion of patients desiccated thyroid will decrease the size of the goiter and lower the basal metabolic rate. The latter may be a result of the iodide in the drug. Iodide causes a favorable response in many patients with thyrotoxicosis, presumably by the inactivation of thyrotropin. The "antihormone" effect produced by pituitary preparations from various species is apparently due to inactivation of the thyrotropic hormone, but the results of this therapy

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The functions of each of these units have a direct or indirect effect on all the others; consequently, it is not surprising that therapy in thyrotoxicosis has been directed at many sites. The main site of action in some instances has not been clearly established.

leave much to be desired. The production of thyroxin is decreased by thyroidectomy, by irradiation of the thyroid gland, and by the administration of thioureas or aminobenzenes. Little progress has been made in obtaining drugs which inhibit the action of thyroxin, although it has been thought that a xanthine derivative has this effect.

Because three relatively good types of treatment, namely, surgery, thioureas, and radioactive iodine, are available for thyrotoxic patients, the question often arises concerning which treatment is the best. In the succeeding paragraphs are listed some factors which help govern the extent of usefulness of the three procedures.

The performance of a subtotal thyroidectomy for the treatment of thyrotoxicosis has one advantage over the use of thioureas or radioactive iodine in that there is more definite information about the long-range results of therapy.

Surgical intervention would seem to be the treatment of choice when there is an extremely large nodular goiter. However, such glands have been observed to decrease slightly in size after the use of thiouracil and to a great extent after treatment with radioactive iodine. In some instances the most rapid relief from the disease is offered by surgical treatment. However, when consideration is given to the time required for the patient to recover completely from the operation, the interval is not infrequently as great as is required for the production of a complete remission with the use of radioactive iodine.

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It has been proposed that an operation is especially desirable when a toxic nodular goiter is present, because of its prophylactic value in the avoidance of the development of malignant changes of the thyroid gland. However, according to Means, whose experience has been with a large and active clinic for the treatment of thyrotoxic patients for a period of more than twenty years, "malignant" neoplasms of the thyroid gland in thyrotoxic patients are extremely rare.

In a consideration of the results of surgical intervention, it must be borne in mind that surgical treatment is available to only a small minority of the people. Consequently, in the assessment of the value of an operation the figures of a few specialized clinics should not be considered as applying to the problem as a whole. Moreover, even in the Massachusetts General Hospital, for example, better results are desirable, for 2.6 per cent of the patients died during or soon after operation, myxedema developed in 2.3 per cent, and hypoparathyroidism developed in 1.3 per cent. Thus far, none of these complications except myxedema has resulted from treatment with radioactive iodine, nor has paralysis of the recurrent laryngeal nerve occurred, and none of them has resulted from the newer thiourea derivatives.

Treatment by means of surgical intervention presents a number of major problems that need not occur with either of the other forms of therapy. The patient must make emotional, financial, and social adjustments for his hospitalization. He is subjected to a great deal of discomfort that is not associated with either of the other forms of treatment. The loss of time from work, nursing care, hospital bill, and surgeon's fee add up to an amount which usually is greater than in the other forms of therapy.

Surgical treatment or the use of radioactive iodine is indicated when an extremely large goiter is present. However, roentgenotherapy used in conjunction with thiouracils has given satisfactory results, particularly if the goiter is not nodular. An operation or radioactive iodine is indicated when serious toxic reactions to thioureas have occurred, although a different derivative of thiourea sometimes may be used satisfactorily. Rarely a patient will appear to be somewhat unresponsive with regard to these compounds, and whereas this refractoriness might be overcome by the use of large doses over long intervals, at present it seems wiser to change to another form of therapy. Radioactive iodine or surgical treatment is preferable for persons in whom it is not desirable to give prolonged treatment, especially in subjects who will not take a thiourea derivative regularly.

Therapy with thioureas or radioactive iodine is desirable especially in the patients who cannot be put conveniently into satisfactory condition for thyroidectomy. These drugs are useful in patients who cannot afford the extra expense of an operation and in those who have a great fear of such treatment. The use of one of the compounds is desirable in persons who have been subjected to one or more thyroidectomies and especially in those in whom a paralysis of the vocal cord has developed or in those with hypoparathyroidism.

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The use of radioactive iodine has the advantage over either of the other forms of therapy in its simplicity of administration and in its effectiveness in essentially all cases. It is distinctly less expensive than surgical treatment and will become much cheaper, but it is available, thus far, to an extremely small number of patients. It is especially useful in patients who are unreasonable and difficult to manage. Moreover, it is probably the most certain way of abolishing thyrotoxicosis, although it is accompanied with a distinct risk of myxedema. The results thus far are promising and doubtless will improve greatly as more information is obtained about the regimen for optimal dosage. At present the results of this form of therapy are more uncontrollable than is true of either of the other types. The surgeon has much difficulty in deciding just how much of the thyroid tissue to leave in even when he has a good view of it. In the estimation of the amount of radioactive iodine to be used, uncertainty occurs concerning how much tissue is present and what the state of iodine metabolism in the patient is, both of which are factors of distinct importance in the determination of the optimal dosage. In general, it seems wiser to err on the side of not giving enough rather than of giving too much, because in the former instance additional doses can be administered. Even though a regimen of multiple dosage is used, it is still possible to overestimate the quantity of radioactive iodine that is necessary. If iodide or a thiourea has been given, it is important to discontinue the former four weeks and the latter one week before radioactive iodine is given. It is advisable to administer one of the thiourea compounds or potassium iodide, or both, during the period of approximately two months following the treatment with radioactive iodine required to obtain a full effect. Hertz has found that when potassium iodide therapy is begun one day after the radioactive iodine has been given the latter is retained to a greater extent.

Concerning radioactive-isotope therapy, two questions are not yet definitely answered: A. Will the gamma rays that are introduced be carcinogenic? Experiences with roentgenotherapy suggest that such an effect will be infrequent. B. What are the damaging effects to other portions of the body, especially the kidney? Another problem which may be presented in the future, with the utilization of the various isotopes in domestic activities, is the avoidance of excess radioactivity.

Therapy with thioureas would seem to offer more opportunity for development than would either of the other types, since many hundred compounds of this type remain unexplored. The rate of production of the thyroid hormone can be much more accurately controlled with thioureas than with surgical intervention or radioactive iodine. Therefore, the level of metabolism can temporarily be adjusted according to what is best for the patient. This regulative ability is sometimes desirable in persons with cardiac disease, anxiety neurosis, and malignant exophthalmos. This type of therapy is available to a larger group of persons than is either of the other types. It is useful in the preparation of patients for thyroidectomy and in those that are not cured by surgical treatment. It is indicated in patients who are waiting for radioactive iodine treatment and in those who are waiting for a response from the latter.

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can be used advantageously when an insufficient amount of radioactive iodine has been given. Indeed, this combined type of therapy might well be superior to any of the other types of treatment. Surgical treatment or radioactive iodine always can be used after therapy with the thioureas if a change is desired. Therapy with thiouracil is more effective in patients with small goiters and slight thyrotoxicosis than in the severer cases. In some patients thyrotoxicosis is a self-limited disease, and in these patients the thiourea derivatives not only can control the manifestations of the disease but may shorten its duration.

Now that many thioureas and aminobenzenes have been studied clinically and many others have been shown to have pronounced antithyroid effects in rats, the question arises what the relative values of these compounds are in the treatment of thyrotoxicosis.

A total of 112 thyrotoxic patients were given two hundred and twenty-two courses of therapy with some of the newer antithyroid drugs. Many of these patients were treated with several courses of therapy, a different compound being used each time, and comparisons were made of the effectiveness of the drugs in the same and in different patients.

On the basis of this study, the following tentative order of decreasing potency of these compounds may be given. There was no definite difference between the effects of 6-propylthiouracil and of 6-cyclopropylthiouracil, but each was more potent than were the other drugs. The next most active was 6-isobutylthiouracil, followed by 6-butylthiouracil, 6-methylthiouracil, thiouracil, ortho-phenylenethiourea, tetramethylthiourea, thiothymine and aminothiazole; last, and much less potent, was para-aminobenzoic acid. In this series not enough experience was obtained with thiourea itself to assess its relative value. Whereas 3,5-diiodo-para-aminobenzoic acid was effective in some cases, it is difficult to determine how much of the effect was due to its iodine content. All the beneficial results obtained from the use of ethyldiiodobrassicinate appeared to be due to the iodine. As far as the clinical application of the compounds is concerned, the order would be somewhat similar, except in the case of a few compounds which caused frequent toxic reactions, as, for example, ortho-phenylenethiourea and aminothiazole. For the same reason the use of thiobarbital is not as desirable.

Whereas Perrault and Bovet were enthusiastic about aminothiazole, 11 per cent of their patients had toxic reactions. Of the patients treated in this series, severe arthritis, fever, and rash developed in 1; in another patient hepatitis developed, but this was probably infectious in origin. Himsworth and Morgans obtained such unfavorable results in the treatment of 13 patients with aminothiazole that they discontinued this form of therapy.

Wilson compared the results of thiouracil treatment of 40 patients with the results of methylthiouracil therapy in 30 patients and obtained better results with the methyl derivative. The experiences with this compound in this series were also fairly satisfactory.

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Although none of the toxic effects of ortho-phenylenethiourea was severe, consisting chiefly in fever, such effects were more frequent than was desirable. Thiothymine was not as active as were many other compounds, and it caused a moderately severe febrile reaction in one patient.

Whereas Berman was enthusiastic about the use of para-aminobenzoic acid, the response of his patients was extremely slow. Moreover, it is not practical to give almost daily intravenous injections for several months. Para-aminobenzoic acid was found not to exert much effect when given orally in large doses. Indeed, it was not satisfactory in the maintenance of the normal metabolic rate which had been produced by derivatives of thiourea. No synergistic effect of para-aminobenzoic acid with thioureas was observed in 2 patients in whom this was tested.

Tetramethylthiourea was found to be a satisfactory drug, but its use occasionally caused a severe febrile reaction.

No significant toxic reactions were caused by 6-isobutylthiouracil, but it was replaced by the propyl derivatives, the antithyroid activity of which seemed to be greater.

Propylthiouracil and cyclopropylthiouracil appeared to be equally active, and neither drug caused any toxic reactions. Consequently, these drugs would seem to be the most desirable ones that are available at present.

The response of some of the patients to the "more potent" thiouracil derivatives was observed to be slow. Indeed, in some of the cases a full response did not occur, but when iodide therapy supplemented the treatment, a complete remission was observed. Whether some of these patients would have shown a full response to a greater dosage of the thiouracils is unknown; some were receiving as much as 200 mg. daily. On the basis of the observations of the antithyroid effects of the propyl derivatives in rats, one would anticipate just as rapid a response in the patients with thyrotoxicosis treated with these compounds as in those treated with thiouracil, provided that an adequate dosage is used. The relatively much greater activity of the propyl derivatives in rats has led to the use of smaller doses of these drugs than are really needed in some cases. By the use of doses slightly larger, toxic reactions might be produced, but this is not necessarily true. On the basis of pharmacologic studies conducted by the author and Kay, it would appear probable that even with the doses of the propyl derivatives which were used, the concentrations of the drugs in the tissues were as great as or greater than those which exist with standard thiouracil therapy.

Whether a greater incidence of sustained remissions will follow therapy with the propyl derivatives than was true of thiouracil therapy remains to be determined. However, there is no good reason for assuming this at present, since the mechanism of action of the two compounds is probably similar.

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It is concluded that in thyrotoxicosis the individual circumstance may determine the treatment of choice, although there are many cases in which the decision is optional and may depend on a number of factors as, for example, the temperament of the patient. In some instances the decision is difficult, but it should become easier as more is learned about the chronic effects of radioactive iodine and of the thioureas. Thiourea derivatives can be used effectively in conjunction with radioactive treatment, or vice versa. It is sometimes of advantage to use all three forms of therapy. (Arch. Int. Med., July '47 - R. H. Williams)

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Radioactive Phosphorus in the Treatment of Blood Dyscrasias: A few radioactive elements have been subjected to therapeutic trial because of their tendency to localization selectively in certain tissues. These are radioactive iodine, radioactive strontium, and radioactive phosphorus (P^{32}). The first of these, radioactive iodine, is concentrated almost exclusively in the thyroid gland and has been utilized with encouraging results in the treatment of Graves' disease and in some cases of carcinoma of the thyroid gland. Radioactive strontium, as well as radioactive calcium, is localized more or less exclusively in bone, and has been employed as a therapeutic agent in neoplastic diseases of this tissue. The therapeutic efficacy of radioactive strontium, however, has been found to be in no way superior to that of other forms of radiation therapy. The third element, radioactive phosphorus, when introduced into the living organism, enters into all phases of phosphorus metabolism. It is concentrated primarily in bone and bone marrow but relatively large amounts also are localized in the liver, spleen, and lymph nodes.

The dosage of radioactive phosphorus is measured in terms of millicuries. One millicurie (mc.) is that amount of radioactive substance of which 37,000,000 atoms disintegrate per second. A microcurie (μ c.) is 0.001 millicurie.

The rapidity of decay of any radioactive substance is expressed by the time required for half of any initial stock of atoms to disintegrate. This is called the "half-life" of the isotope. In the case of radioactive phosphorus, through the emission of a beta particle, thirty-five out of every million atoms undergo spontaneous transformation to stable sulfur each minute, giving radioactive phosphorus a half-life of 14.3 days.

In contrast to radium which emits alpha, beta, and gamma rays, radioactive phosphorus emits only the electron (beta ray). The depth of penetration of the beta ray varies in different tissues; the maximal range of penetration is approximately 7 mm. The beta ray has the capacity to produce ionization in tissues, and therefore its radiation effects are basically similar to those of roentgen rays and of radium.

Radioactive phosphorus is chemically indistinguishable from ordinary stable phosphorus and, therefore, enters into all phases of phosphorus metabolism

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in the same manner as does the natural element. After administration it is rapidly and selectively withdrawn from the blood by certain tissues and cells. According to Reinhard and his co-workers the selective uptake of phosphorus by cells is dependent principally on three factors: (1) the total amount of phosphorus in exchangeable form in the tissue; (2) the rate of turnover of phosphorus by the tissue, and (3) the rate at which new tissue is formed.

As stated previously, in normal animals radioactive phosphorus is deposited in large amounts in bone and bone marrow, and in somewhat smaller quantities in liver, spleen, and lymph nodes. Under pathologic conditions, the uptake has been found to be much higher in rapidly metabolizing neoplastic tissues than it is in the same type of normal tissue.

In leukemia and in polycythemia, P^{32} is taken up rapidly by both circulating erythrocytes and leukocytes during the first twenty-four hours after administration. The concentration in erythrocytes then falls sharply, but the concentration in leukocytes falls more slowly and the P^{32} is retained for much longer periods and in greater quantities than in the erythrocytes.

In certain diseases of the hematopoietic system the distribution of P^{32} in various organs and tissues has received considerable attention. In chronic myelogenous leukemia greater activity was found in the bone marrow than in any other organ, whereas in chronic lymphatic leukemia the liver, spleen, and lymph nodes in most instances contained a higher concentration of P^{32} than did the bone marrow. In acute leukemia or leukosarcoma varying results were observed, but in general, more of the material accumulated in the liver and spleen than in the bone marrow. In most cases, however, the concentration of P^{32} was found to be lower in lymph nodes than in bone marrow, liver, spleen, or kidney. In lymphosarcoma and actively progressing Hodgkin's disease, Erf and Lawrence found as great a retention of P^{32} in lymph nodes as in the liver and kidney. However, in one case of Hodgkin's disease in which the lymph nodes had become densely fibrotic, the uptake of P^{32} was less than in the other tissues assayed.

Data concerning the differential uptake of P^{32} in various organs in other diseases also have been accumulated. These diseases include melanoma and melanosa, seminoma, neuroblastoma, Ewing's sarcoma, fibrosarcoma, reticulum cell sarcoma, multiple myeloma and metastatic carcinoma. In general, the distribution of the substance among different organs and tissues of the body depends on the type of neoplastic disease present, the degree of infiltration of an organ with abnormal cells and the rate of growth of these cells. Tissues having a high concentration and a rapid turnover of stable phosphorus also take up higher concentrations of P^{32} than do normal tissues.

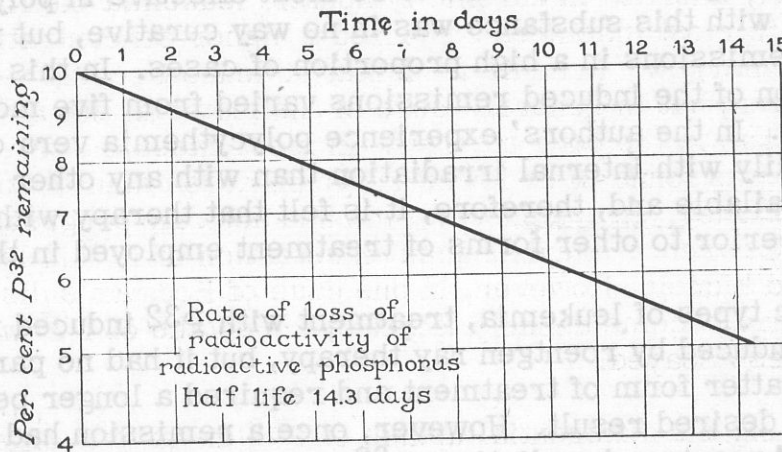
Radioactive phosphorus may be administered to patients either orally or intravenously. When the oral route is employed, from 15 to 50 per cent of the amount administered is excreted in the urine and feces during the first six days. Most of this loss is due to a lack of absorption in the gastro-intestinal tract.

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As a general rule, it is safe to assume that 25 per cent of the amount of P^{32} administered orally will be lost in the stool and that 75 per cent will be absorbed.

When P^{32} is administered intravenously to normal subjects, from 25 to 50 per cent of the quantity injected is excreted during the first six days. In leukemic and polycythemic patients the excretion of the isotope is less than that in normal individuals, varying from 5 to 25 per cent of the amount injected over a similar period of time. With the intravenous route of administration most of the loss occurs in the urine.

The authors' studies of treatment with P^{32} began in the fall of 1941. The isotope was supplied to them as an isotonic solution of dibasic sodium phosphate, containing 15 mg. of the salt per cubic centimeter of solution. On receipt, isotonic saline solution was added so that the specific activity of 1 c.c. was 1 mc. The material, in a rubber-stoppered vaccine bottle, then was autoclaved at a pressure of 50 pounds (250° F.) for one hour. Intravenous administration was utilized in all cases because studies have shown that thereby a more accurate relationship can be maintained between the amount retained and the dose administered than is possible with the oral route. For oral administration sterilization is not required, but the material should be stored in the icebox to prevent the formation of mold.



In order to calculate the correct dose to be administered to a patient, the physician must know the rate of decay of the isotope. The rate of loss of radioactivity follows a constant pattern that can be plotted on logarithmic paper as a straight line (see chart above). The specific activity per cubic centimeter of solution then can be read directly from the chart at any given time after the initial determination of potency. For example, a specimen containing 1,000 microcuries of P^{32} per cubic centimeter of solution will have a specific activity of 950 microcuries per cubic centimeter at the end of twenty-four hours, 908 microcuries at forty-eight hours, 864 microcuries at seventy-two hours, and so on. It thus becomes a simple matter to translate specific activity into cubic centimeters of solution for any dose of P^{32} .

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Throughout this investigation the authors intentionally restricted the use of P^{32} as a therapeutic agent to diseases in which the bone marrow was involved primarily by a pathologic process, or to diseases in which the marrow was extensively involved even though the primary site of the disease was in other organs. One hundred and forty-three patients were treated as indicated in the table below.

Disease		Cases
Polycythemia vera		97
Myeloma		22
Myelogenous leukemia (17 cases)	Chronic	15
	Acute	2
Lymphatic leukemia, chronic		3
Monocytic leukemia (2 cases)	Chronic	1
	Subacute	1
Hodgkin's disease of bone marrow		2
Total		143

Radioactive phosphorus was found to be most effective in polycythemia vera. Treatment with this substance was in no way curative, but resulted in the induction of remissions in a high proportion of cases. In this series of cases, the duration of the induced remissions varied from five months to nearly four years. In the authors' experience polycythemia vera can be controlled more readily with internal irradiation than with any other therapeutic procedure now available and, therefore, it is felt that therapy with radioactive phosphorus is superior to other forms of treatment employed in the past.

In the chronic types of leukemia, treatment with P^{32} induced remissions similar to those induced by roentgen ray therapy, but it had no particular advantage over the latter form of treatment and required a longer period of time to bring about the desired result. However, once a remission had been induced by means of roentgen irradiation, P^{32} was found to be effective in holding leukocyte counts near normal for long periods of time. Used in this way, P^{32} eventually may prove to be a useful adjunct to treatment with roentgen rays.

Radioactive phosphorus was ineffectual in inhibiting the progression of acute leukemia, Hodgkin's disease, and multiple myeloma. However, in myeloma, treatment with the isotope afforded varying degrees of relief from pain in the bones in more than 50 per cent of this series of cases. In one case of myeloma the observation that treatment with P^{32} , combined with roentgen-ray therapy, resulted not only in destruction of the tumor tissue locally but in the formation of new bone at the site of the original tumors, has proved of sufficient interest to warrant further study. Consequently, an investigation of the effects of combined therapy now is being carried out.

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Treatment with radioactive phosphorus is not a difficult procedure, provided the therapist knows the rate of loss of radioactivity and the rate of excretion of the isotope. Dosage then can be adequately controlled. The chief advantages of this form of therapy are the ease of administration, the absence of radiation sickness and toxic symptoms, and the concentrated effect of the irradiation on the cells of the hematopoietic organs. The principal disadvantages of the method are that (1) because radioactive phosphorus enters into all phases of the metabolism of phosphorus in the body, tissues other than those one wishes to treat are irradiated, and (2) if an overdose of the isotope is administered, no effective method is available for inhibiting or stopping the irradiation effect. Leukopenia, thrombocytopenia, and anemia can be produced, and in order to prevent severe damage to the bone marrow, adequate observation and carefully controlled dosage are essential. (M. Clin. North America, July '47 - B. E. Hall and C. H. Watkins)

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Earlier Ileostomy in Severe Ulcerative Colitis: When patients in the acute stages of ulcerative colitis are permitted to go on to the point where everyone connected with the case - surgeon, physician and the patient's relatives - agrees that the patient must have an ileostomy in order to save his or her plainly threatened life, the mortality of the procedure will be, as it has been, distressingly high.

It is unfortunate that several factors operate to bring about delay in these often severely ill patients. Sometimes they have been through previous acute episodes of ulcerative colitis, have spontaneously recovered, and have had varying periods of remission from the bloody diarrhea together with the fever and toxicity associated with it, thus encouraging them to persist unduly with conservative measures again during subsequent acute episodes. Sometimes the mixed infections superimposed upon these acute ulcerative processes previously have been controlled by sulfasuccinate or some of the other intestinal antiseptics of the sulfa group, again encouraging delay and undue dependence upon these agents. Sometimes the physician in charge of a patient in such an acute stage of the disease has not had enough experience with it to be aware how quickly patients with relatively well controlled ulcerative colitis can, with but little apparent cause (emotional upsets or associated infections such as influenza), change to states which are real emergencies, such as, bleeding from the colon which can threaten life by exsanguination, progress of the ulcerative process which can and does bring about perforation, toxic states as the result of the colon infection which threaten life by the intensity of the infection, and nutritional changes and avitaminosis as the result of the frequent loose stools which bring about serious prospects of a fatality.

Added to the above stated deterrents to an early ileostomy is the fact that until recently a patient with an ileostomy was one to be really pitied since there was no adequate way of controlling either the character or the frequency of the liquid discharges from the ileostomy, no bag which would really prevent soiling

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of clothes or odor, and in many of the cases the skin about the ileostomy was badly irritated by the discharges from the ileum. In spite of all protective measures, patients have been constantly disturbed and distressed by an ileostomy.

All of the features of this distressing and serious disease so prejudiced patients, their relatives, surgeons, gastro-enterologists, and physicians against this enterostomy that it was delayed, in a great many cases with considerable justification, until the patient's condition was so desperate that, with all of the objectionable drawbacks, ileostomy was accepted rather than the impending and obvious fatality about to occur. Evidence of the truth of these statements is the fact that at the Lahey Clinic, in the first 80 patients upon whom ileostomy was done, the mortality rate was 26 per cent, the direct result of the lateness in the acute stage of the disease with which these patients were submitted to ileostomy.

It is because almost all of the drawbacks previously and rightly charged to ileostomy have been overcome that the author wishes to urge earlier ileostomies, followed in many cases by later partial or complete colectomies. The Lahey Clinic has advocated and practiced early ileostomy for any patient not doing well under medical management, and has been committed to the program of disconnecting the ileostomy and restoring the fecal stream under the following conditions: when, following the ileostomy, the patient has remained free from all symptoms for a considerable time; when haustrations as shown by barium enemas have returned to normal in the colon; when by sigmoidoscopic examination the lower bowel and rectal mucosa become normal in appearance; and when, in addition, the patient and family understand that the restoration of the fecal stream may reactivate the ulcerative colitis process and make another and permanent ileostomy necessary.

Many patients with ulcerative colitis may be satisfactorily maintained on a medical regimen (diet, psychogenic control, and typhoid vaccine), but when these measures no longer prove satisfactory, the Lahey Clinic urges and practices earlier ileostomy in these patients and has convinced its gastro-enterologists and medical consultants of the wisdom and life-saving value of this, particularly since the Koenig-Rutzen bag has become available, and since the Clinic has been able to offer these patients the possibility of closure of their ileostomy and restoration of their fecal stream in properly selected cases. The Koenig-Rutzen bag is now known to almost everyone, but for the benefit of any who do not know about it, it is a bag so made with a flanged cuff that it can be so accurately cemented to the skin about the ileostomy that there is no exposed skin left to become irritated. The character of the cement is such as to hold the bag firmly fixed to the skin so that a watertight seal, impervious to the liquid discharges from the ileum, results. The bag has a spigot at its bottom which can be folded over and closed with rubber bands and opened so that the contents of the bag, when it becomes filled and heavy, can be drained off into a toilet. It permits every activity its wearer desires and its availability now obviates any excuse for delay in the employment

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of ileostomy as a life-saving measure in patients who are in acute phases of ulcerative colitis with hemorrhage from the colon, highly toxic states as the result of progressive infection in the colon, dangerous nutritional states, threatened perforation and frequently joint involvement (acute arthritides), weight loss, and severe secondary anemias.

It is not the purpose here to discuss the many technical features which go with doing an ileostomy, its care, and when to follow it with colectomy, partial or complete, but to call attention forcefully to the fact that with the ability to disconnect the ileostomy and to restore the fecal stream in proper cases, and with the complete comfort and happiness a patient now can have with a Koenig-Rutzen bag, the factors which led to such a high mortality rate in the past in these patients have largely been overcome. In patients with earlier ileostomies for ulcerative colitis, the mortality rate at the Clinic has now been reduced to 2 per cent. (Surg., Gynec., and Obstet., Aug. '47 - Editorial, F. H. Lahey)

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The Hyperventilation Syndrome: The syndrome resulting from hyperventilation is an important medical condition, yet one which is often unrecognized. Until recent years the mechanism of this disorder has been poorly understood.

Etiology. The symptoms of the hyperventilation syndrome come about as the result of an increased loss of carbon dioxide from the body. This occurs from the lungs in the course of an excessive pulmonary ventilation. The **usual concentration of carbon dioxide in the alveolar air is approximately 40 mm. partial pressure of mercury.** With unduly stimulated breathing this **level of alveolar carbon dioxide may be reduced to approximately a half of that value.** Thus a chain reaction is initiated which in turn affects the equilibrium existing between the carbon dioxide of the alveoli and of the blood, and subsequently that **equilibrium existing between the carbon dioxide and the bicarbonate of the blood.** An increased alkalinity is made temporarily present in **the blood as the so-called respiratory alkalosis** is brought about. Numerous chemical changes occur in the body as a result of this respiratory alkalosis. Grant and Goldman recognized in 1920 that tetany could be induced by means of hyperventilation. This effect is mediated through the influence of respiratory alkalosis on the blood calcium. Although no significant change in the total calcium of the blood takes place, the readily available, or ionized, portion is affected markedly. This ionized calcium is, in part, temporarily bound by the increased alkalinity present in the blood in respiratory alkalosis. The decrease in available calcium increases the excitability of the neuromuscular mechanism, thus inducing tetany.

Recently it has been stressed that respiratory alkalosis will significantly alter the release of oxygen from hemoglobin within the tissues of the body. With a lowered carbon dioxide pressure in the blood, hemoglobin clings more

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tenaciously to its bound oxygen. Less oxygen is relinquished in the tissues as the blood passes through. Another factor which interferes with tissue oxygenation is the decreased blood flow as a result of contracted blood vessels in tissues low in carbon dioxide pressure.

Clinically, the hyperventilation syndrome may occur in many forms and all forms have, in common, increased pulmonary ventilation. This respiratory abnormality may be observed in entirely stable subjects, particularly when they are exposed to emotional stress. Most commonly, however, this syndrome is observed in tense, excessively anxious, depressed, or psychoneurotic patients. Such subjects often fall into the practice of hyperventilation when placed in a situation where embarrassment would be experienced should fainting occur, such as in crowds, in a front pew in church, or preoperatively in a hospital. At such times the respiration may be increased in depth, accelerated, or both, with the insidious onset of symptoms referable to respiratory alkalosis. Such patients will realize that something is amiss and will attempt to fight off their unpleasant symptoms through further hyperventilation by forced breathing.

Alkalosis may be induced by unrecognized stimulation of respiration as described. The frequent sighing observed in tense subjects may contribute to the production of a lowered concentration of carbon dioxide in the blood (acapnia). Experimentally forced breathing will reproduce the symptoms of respiratory alkalosis. It may well be that strenuous exercise by those unaccustomed to it will lead to acapnia; particularly is this true of swimming, an activity imposing a voluntary influence on an involuntary center for respiratory regulation. Physical activities at altitudes at which oxygen pressure is decreased may lead to a washing out of the carbon dioxide of the body more rapidly than this gas can accumulate through metabolic processes.

Symptoms. Following World War I, White and Hahn studied large groups of subjects with and without the so-called effort syndrome. They observed sighing dyspnea in 80 per cent of such subjects. In a healthy group of controls this breathing irregularity was observed in but 19 per cent. They concluded that hyperventilation was responsible for the symptoms of this condition. In 1938 Soley and Shock likewise observed that hyperventilation was responsible for the symptoms of the effort syndrome. They substantiated their conclusions by carefully controlled physiologic studies of the changes occurring in the blood and alveolar air.

Gliebe and Auerback have emphasized the frequency with which hyperventilation may simulate organic disease. They have observed hyperventilation as a part of the fear reaction in emotionally unstable persons. Confronted by a situation in which he is inadequate, a patient may transfer his anxiety to any organ by a sequence of physiologic changes resulting from hyperventilation. Thus the precipitating psychic conflict may be ignored entirely as the patient pursues an explanation for his somatic symptoms.

The importance of hyperventilation as the so-called trigger mechanism in precipitation of manifestations of hysteria has also been emphasized. It

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is probable that hyperventilation contributes to the so-called acute anxiety attack.

Because subjects who are otherwise quite stable will become subject to hyperventilation in times of anxiety or fear, this disturbance of respiration becomes of utmost importance in aviation. Faulty judgement and in-co-ordination in the course of overbreathing are causes of failure in pilots.

The symptoms of respiratory alkalosis are insidious and minimal in their onset, but, if measures are not taken to rectify this abnormality of breathing, they may assume an alarming character. If the patient understands his condition poorly, these symptoms may induce a state of panic as he realizes that something over which he has no control is happening. An early symptom is that of lightheadedness and unsteadiness. This is entirely subjective in its beginning. As the alkalosis progresses, a sense of a vacuum which is insatiable by the deep breathing it prompts is produced in the thorax. Patients may fan themselves and glance around for the nearest exit. Often they will go out of doors or open a window in an attempt to secure more adequate respiration. In the thorax a sense of dull pressure is often noted. This often leads to anxiety concerning the heart. For the examining physician such distress makes obvious the necessity for great care to exclude the pain arising from coronary artery disease.

With further hyperventilation a sense of numbness and tingling in the extremities and around the lips develops. Ultimately these pretetanic paresthesias are followed by spontaneous muscular twitching and then tetany of a carpopedal type. Throughout this sequence of physical changes mental astuteness is lost gradually and the loss is first apparent only in its effect on judgement and skill, but ultimately it progresses in some cases to stupor.

Diagnosis. Through recognition of the manifestations of hyperventilation, the diagnosis can be made readily. Should the patient be examined by a physician at a time when evidences of respiratory alkalosis are not present, the characteristic history will be the guide to a correct appraisal of the patient's complaint. Under such circumstances, the symptom of which the patient complains frequently may be reproduced by a period of forced breathing sufficient to induce respiratory alkalosis. Three minutes of moderately accelerated breathing with care to exhale the supplemental air usually will suffice. Often only a part of the patient's symptoms may be reproduced, the deficit being attributable to the lack of a fear response associated with the release of epinephrine within the body.

Treatment. Treatment of the hyperventilation syndrome depends largely on its diagnosis which enables the physician to offer an explanation of the condition to the patient. By avoiding the practice of forced breathing, by temporarily holding the breath, or by rebreathing air exhaled into a paper sack, the patient may bring about alleviation of his symptoms within a few seconds. Nasal,

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instead of oral, breathing likewise is of value in overcoming respiratory alkalosis. By means of these measures carbon dioxide is allowed to reaccumulate in the alveolar air. The most anxious patient appreciates the physician's demonstration that the terrifying sensations are not imaginary. He develops confidence that his condition is understood and becomes willing to discuss any underlying psychic factor. In many cases it is only necessary to demonstrate that the symptoms are the result of hyperventilation and to explain the nature of these symptoms to the patient. In other cases, the anxiety is more deeply motivated and prolonged psychiatric investigation and treatment may be indicated.

The recognition of the hyperventilation syndrome represents a means of explaining symptoms long known to be functional in origin but little understood. This knowledge has provided a way of adequately treating a previously unsatisfied group of deserving patients who "know something is wrong." (M. Clin. North America, July '47 - H. M. Carryer)

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Concentrated Aqueous Heparin: This communication describes the clinical utilization of a new preparation of concentrated aqueous heparin which can be administered intramuscularly. It has proved valuable in inhibiting coagulation in thrombophlebitis, phlebothrombosis, postoperatively as prophylactic therapy against venous thrombosis, and as an adjuvant to the use of dicumarol in various thrombotic states. Although the total number of cases (115) treated is small and inadequate for statistical analysis, the experience in this series has shown that the use of the drug by this simple technic has merit.

Studies with the intramuscular administration of heparin in the dilute solution (10 mg. per c.c.) commercially available, led to the use of a concentration of 100 mg. in 1 c.c. Such a solution of concentrated aqueous heparin, free from foreign substances or the vasoconstrictor agents, and watery in appearance and viscosity, was administered intramuscularly under the authors' supervision for about a year. The medication was usually injected by nurses into the gluteal muscles with the regular intramuscular syringes and needles at from 8- to 12-hour intervals. Individual doses of heparin varied from 50 to 180 mg., the smallest doses being given to patients weighing 90 pounds or less and the largest to those over 180 pounds. At the present time the data are not complete enough to permit the formulation of exact schedules of administration, for patients vary in their requirement of heparin. No attempt was made to ascertain the reasons for this except to observe a rough correlation of requirement with body weight. Adequate prolongation of the coagulation time of the blood is usually attained in patients weighing between 100 or 130 pounds by administering 100 mg. every 8 hours or from 120 to 140 mg. every 12 hours. In heavier individuals larger doses may be required. The maximum daily dose should not exceed 450 mg. The successful heparinization in patients weighing over 170 pounds may be obtained by giving 1 mg. of heparin per pound of body weight as the initial dose, and between 0.5 and 0.7 mg. of heparin per pound at 8-hour intervals subsequently.

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The medication was administered postoperatively over a period of several months to most of the patients of a general surgical service, including a considerable number of those who had had thoracic surgery, and sympathectomies for hypertension. The cases were not selected; the ages varied from 17 to 70 years, (though the majority of the patients were over 40 years), and both sexes were included. Many of the patients were febrile and received other medication such as vitamins, blood transfusions, sulfonamides, or penicillin. The nutritional and metabolic status of several of the patients was poor since a considerable number with carcinoma were included in this series. Almost all were in bed. The administration of heparin was usually started from 24 to 72 hours after operation and was continued for a varying period or until the patients were out of bed and walking. In a first group of 90 patients there was no existing intravascular thrombosis, nor did venous thrombosis develop. Bleeding at the site of operation was observed several days after beginning heparin in 3 cases early in the series. It was found that this complication could be averted if the anticoagulant were withheld until from 48 to 60 hours had elapsed after operation. In a second group of 25 patients, most of whom had recently experienced thrombophlebitis or coronary artery thrombosis, bleeding was not observed. Hemorrhage into an internal organ was never observed.

One of the practical advantages of this method of heparin administration is the ease with which the anticoagulant effects can be controlled. In the first trials the coagulation times (Lee and White method) were performed at frequent intervals in order to insure an adequate but not extreme anticoagulant effect. At the present time one coagulation determination daily, immediately before the administration of a dose, is found to be adequate. If the result of this test reveals complete cessation of heparin effect, a dose somewhat larger than the previous one is given. If, on the other hand, a satisfactory prolongation of the coagulation time (from 18 to 24 minutes) is observed, the dosage is not changed. If the coagulation time is found to be over 24 minutes, either a smaller dose is ordered or the injection is postponed for 2 hours. Coagulation tests done at other intervals after injections reveal prolongation beginning from 1/2 to 1 hour after the initial injection. The greatest prolongation is observed from 4 to 6 hours after an injection, and, with the doses of heparin which were administered in this series, varied between 25 and 60 minutes. Prothrombin or other determinations are not required.

The injections were given with the usual syringes and 20-gauge, 1 and 1/2 inch needles. This technic was followed in order to maintain the customary ward routine. Since the heparin is in an aqueous medium, it can be given easily with 22- or 24-gauge needles. In only rare instances did a hematoma appear at the site of injection and this was never large. A reaction which occurred in 2 per cent of the injections consisted of a palpable and occasionally tender nodule up to 3 cm. in greatest dimension. Frequently the patients were not aware of these nodules which were absorbed despite continuation of the drug. In a small number of instances included in the above, nodules were not palpable, but patients complained of some pain at the site of injection. This was never severe enough to require analgesics.

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In the small series of patients with thrombophlebitis treated with heparin, the same rapid subsidence of fever, tenderness, and edema in the affected extremity was observed as that described by others who used different preparations of heparin or other anticoagulants. Some of these patients were treated for periods as long as 3 weeks.

Advantage of the prompt action of heparin was taken in administering it to 10 patients who were concurrently treated with dicumarol. Approximately 48 hours after the commencement of the conjoint therapy, the heparin was discontinued when the prothrombinopenic effect of dicumarol was evident. (Am. J. M. Sc., Aug. '47 - D. Stats and H. Neuhof)

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Differential Diagnosis of Cardiac Pain Caused by Coronary Insufficiency:

The clinical characteristics of a classical attack of angina pectoris or coronary occlusion are so well known that their repetition here might seem unnecessary; however, too much emphasis cannot be placed on recognition of the usual pattern of pain resulting from insufficiency of the coronary arteries. Most often, the pain is described as a sense of pressure; but it may be a sense of constriction, a burning sensation as though a hot iron were introduced deep under the sternum, a severe aching sensation, or the feeling that "something is about to burst." Rarely is the pain sharp or lancinating, and never is it momentary. The pain appears to be deep and is not accompanied by tenderness of the superficial tissues. It is located under the upper portion of the sternum and if it originates in other parts of the chest, it almost invariably extends to the substernal area. The pain may spread laterally from the substernal area, not infrequently extending down the inner aspect of the left arm. Less frequently it radiates down the right arm, or occasionally it may be felt in both arms. Other regions to which the pain may extend are the throat, the jaws, the back of the neck, and the region of the upper dorsal spine. The pain at times originates in the aforementioned areas and on occasion may be felt there alone; however, the greatest caution must be exercised, when such is the case, before incriminating the coronary circulation as the primary source of the disorder. Perhaps the most characteristic quality of the pain is its relation to effort. At the onset the pain almost invariably follows some unusual type of effort such as shoveling snow, rapid walking on a cold morning, pushing a disabled automobile, or carrying some unusual load. The pain comes on with effort, not following it as is so often the case in neurasthenia. As the condition progresses the pain may result from emotional excitement.

Coronary disease is infrequent in women under the age of 50, whereas neurasthenia and cardiac anxiety are frequently seen in this age group. Coronary disease may occur in men in the early thirties or even the twenties, and yet its occurrence is rare enough so that every serious consideration should

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be given to the symptomatology before the diagnosis is made.

There are many patients, however, who complain of chest pain which does not fit the pattern described and in whom it is difficult to determine the cause. The problem is important because of the frequency with which patients complain of "pain over the heart." An unwise statement, an equivocal remark, or the unwarranted use of digitalis may create an anxiety state far more disabling than organic heart disease. It seems worth while, therefore, to discuss some of the conditions that may give rise to symptoms simulating the pain of coronary insufficiency and to emphasize some of the points in the differential diagnosis.

The pain resulting from a functional disorder of the stomach or intestine is often located beneath the lower portion of the sternum and across the lower chest. It is described as a sense of pressure or distention and is ordinarily not as severe as that seen with coronary heart disease. It is usually not of short duration and is not definitely related to effort in that it cannot be produced at will by effort and does not stop shortly after the cessation of effort. Pain from an irritable bowel is usually accompanied by other signs and symptoms, such as constipation, excessive flatulence, belching, and abdominal tenderness. Finally, proper attention to the bowel complaints usually will relieve the chest pain or at least render it less severe. The age, sex, and emotional stability of the patient are important considerations.

Pain arising from a hiatus hernia may simulate the pain from coronary insufficiency and should be considered whenever chest pain is atypical. Ordinarily, the pain of a hiatus hernia is expected to come on with recumbency and to be relieved by getting up and walking. However, anything that forces a portion of the stomach through the hiatus will bring on the pain. It may come on with effort and occasionally it occurs with psychic and emotional stimuli. The roentgenologic examination is the key to the diagnosis in these cases, but it should be pointed out that an ordinary roentgenologic examination of the stomach may not reveal a hiatus hernia; fluoroscopic examination with the patient in the recumbent position usually is required for such a diagnosis. It is important to recognize the presence of a hiatus hernia because of the satisfactory results to be obtained from surgical correction of the condition.

Esophageal spasm may give rise to pain which in location and type is difficult to distinguish from that due to coronary disease. It may be relieved by administration of nitroglycerin which adds to the diagnostic problem. Pain from esophageal spasm is usually attended by difficulty in swallowing and tends to last longer than anginal pain. Esophageal pain is likely to begin while the patient is eating rather than with effort after eating. It may start with the swallowing of some rough particle of food such as popcorn. Observation of the patient under the fluoroscope while he is swallowing thick barium may aid in the diagnosis.

Occasionally a congested liver will give rise to pain located under the lower portion of the sternum that is not unlike anginal pain in that it may

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come on with exertion and be relieved by rest. The finding of an enlarged, tender liver and other evidence of congestive heart failure will aid in differentiating the two conditions. Here again proper management of the congestive failure will alleviate the condition.

Much has been written with regard to the differentiation of the pain resulting from cholecystitis and that of coronary insufficiency. The problem becomes more difficult when the two conditions coexist, in which case a gall bladder attack may provoke an attack of pain from coronary insufficiency. Generally speaking, the pain in gall bladder disease is upper abdominal rather than substernal, and it tends to radiate to the lower scapular area rather than to those areas described for coronary insufficiency. The pain is more colicky in nature rather than continuous and it tends to last longer. The exciting factors usually are different in the two conditions, the attack of cholecystitis being related to particular types of food, and the attack resulting from coronary insufficiency being related to effort. The electrocardiogram and the roentgenogram may provide aid in the differential diagnosis, but there are limitations to the information that may be derived from these procedures. This is especially true when an acutely inflamed gall bladder is to be differentiated from a myocardial infarct in order that surgical intervention may be carried out at an optimal time. It may be thought that enough time has not elapsed for changes in the electrocardiogram to have taken place should an acute myocardial infarct be present. The presence of fever, abdominal tenderness, or rigidity, and a high leukocyte count are evidence in favor of an acute cholecystitis. When there is doubt concerning the diagnosis, a few hours of watchful waiting are to be recommended rather than hasty surgical intervention.

At times patients with osteo-arthritis or spondylitis of the thoracic spine have attacks of substernal pain which are to be differentiated from that due to coronary insufficiency. This pain frequently awakens the patient at night, especially if he sleeps on a soft mattress. It tends to occur more commonly in women, especially in the postmenopausal period. The pain tends to radiate around the ribs toward the spine rather than to the arms or throat. It is not related to effort and frequently will be relieved if the patient gets up and walks. The presence of degenerative changes shown in the roentgenogram of the dorsal spine, especially in the region of the neural foramina, and the lack of characteristic electrocardiographic findings for a myocardial infarct, aid in arriving at the diagnosis. A somewhat similar pain may arise from intraspinal lesions which will require neurologic evaluation from coronary pain. A lumbar puncture which reveals a block in the flow of spinal fluid or increased protein content in the spinal fluid may contribute valuable evidence in favor of a neurologic lesion.

The pain arising from acute fibrinous pericarditis may so closely simulate that of coronary occlusion that frequently an erroneous diagnosis of myocardial infarction is made. Pericarditis should always be considered when a young person is seized with severe pain in the chest that has the distribution of pain arising from a myocardial infarct. A pericardial friction rub may assist in the diagnosis of pericarditis but so often it is present for such a short time

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that it is missed. The physician must bear in mind that it can and does occur with a myocardial infarct. Considerable reliance can be placed on the electrocardiogram in the case of pericarditis. One of the most characteristic features is the speed with which the electrocardiogram returns to normal as the patient recovers. Pleurisy involving a region near the pericardium can usually be distinguished by its tendency to disappear with deep inspiration. Acute mediastinal emphysema may give rise to severe substernal pain, but this condition can be differentiated from coronary pain by the presence of a characteristic clicking sound synchronous with respiration.

A dissecting aneurysm of the aorta is difficult to differentiate from a myocardial infarction especially since it is so likely to end fatally before electrocardiographic changes could have been expected from a myocardial infarction. The pain in a dissecting aneurysm of the aorta is described as excruciating and tearing in character, and morphine does not relieve it as successfully as in the case of myocardial infarction. The pain associated with a dissecting aneurysm radiates through to the back and is usually attended by neurologic symptoms owing to interference with the blood supply to the spinal cord. These symptoms include paresthesias, later followed by actual anesthesia in the involved area. In some cases the patient survives one or more dissections. This condition should be considered when characteristic electrocardiographic changes do not occur following an episode of pain as described previously.

Finally, there remains the nervous, hypersensitive, anxious patient who has sharp stabs of pain usually in the region of the cardiac apex without definite relation to effort. In many cases these are somatic pains, the exact mechanism of which is not entirely clear nor is it known why they occur on the left side of the chest more frequently than on the right side. The location, momentary character of the pain, the lack of characteristic radiation, and the age, and sex of the patient will help to distinguish this condition from the pain of coronary insufficiency. Often a cause for cardiac anxiety can be elicited, such as the death from heart disease of a close relative or friend. It is in these cases in particular in which a thorough examination should be made and in which the physician should be especially careful not to add to the cardiac anxiety.

The characteristic history of pain of the type which occurs with coronary insufficiency, its definite relationship to effort, and the tendency for the disease to occur in men lay the foundation for an accurate diagnosis. Additional help can be obtained from the electrocardiogram, especially by the use of multiple precordial leads. When this alone is not sufficient, the exercise test of Master, or the anoxemia test of Levy may provide valuable additional information. There remains, however, the occasional case in which the history and findings are inadequate to explain the symptoms. It is in this type of case that a policy of watchful waiting is necessary; physical activity should be restricted to a safe level, nitroglycerin should be employed as a therapeutic trial, and

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above all, undue cardiac anxiety must be avoided. (Lahey Clin. Bull., April '47 -
D. I. Rutledge)

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The Functions of the Connective Tissue: In recent years, increasing attention has been devoted to the investigation of the specific physiologic functions of the connective tissue, factors which affect its activity, and chemical and pathologic changes which are found associated with it in various disease processes.

Besides its role as a supporting structure, the connective tissue has been described as a semipermeable barrier between the canalicular vessels and the parenchymal cells, as a depot for the storage of nutrient materials and as a regulator of the water and salt balance of the body. In addition, plastic and protective activities, such as healing of wounds, and antibody formation, have been considered as functions of this tissue.

Extracellular substances found in the space between the blood vessels and the parenchymal cells are believed to be products of mesenchymal cellular activity. Several of these substances have been isolated and their properties partly identified. The greater portion of the protein component of connective tissue has been found to consist of collagen; elastin and reticulum are also present. Chondroitin sulfuric acid and hyaluronic acid are the most extensively studied polysaccharides; other sulfuric acid esters of polysaccharides have been described by Dr. Karl Meyer and others.

Hyaluronic acid has been isolated in significant quantities from synovial fluid, aqueous and vitreous humors, Wharton's jelly, and skin. Hyaluronic acid is also present in the capsules of certain streptococci, and is believed to be present in the jelly-like material surrounding the ovum as it is extruded from the ovary.

Hyaluronidase, which depolymerizes hyaluronic acid, occurs in the mammalian testis, eye and skin, many pathogenic bacteria, poisonous insects, leeches, and snake venoms. This enzyme complex is believed to be present in an inactive form in the skin. Hyaluronidase is identical with the "spreading factor" of Duran-Reynals and can be demonstrated to increase the area of spread of intradermally injected particulate substances such as India ink, dyes, viruses, and bacteria. This spreading is made possible by the depolymerization of the gel-like hyaluronic acid in the connective tissue.

Many factors have been reported to influence the composition and activity of the connective tissue. Among these, sex, age, hereditary background, and hormonal influences have been listed.

In recent years, many interesting concepts have emerged from studies of mesenchymal diseases. Klemperer, Pollack, and Baehr have emphasized that

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the connective tissue is the tissue primarily involved in the so-called diffuse collagen diseases. The latter include disseminated lupus erythematosus, scleroderma, and rheumatic fever. These authors have pointed out that the response to certain noxious stimuli may be collagenous rather than cellular (e.g., keloid formation).

Rich has postulated that anaphylactic hypersensitivity may be a factor in the development of the typical lesions of a variety of mesenchymal diseases. This view is supported by the work of Rössle and of Jaeger who pointed out that fibrinoid degeneration is a constant and characteristic feature of diseases of allergic type. Selye and others consider that certain endocrine factors, especially those involving the pituitary-adrenocortical axis, may be important in the pathogenesis of certain connective tissue diseases. Selye has succeeded in the experimental production of Aschoff nodules, lesions typical of periarteritis nodosa, and lesions suggestive of rheumatoid arthritis by administration of large doses of desoxycorticosterone acetate.

It is believed that study of the basic chemistry and physics of the connective tissue will lead to further understanding of the behavior of this tissue in health and disease and will make possible the correlation of available information. The observation of Watson and Pearce on pretibial myxedema, reported in the current issue of the Journal, is a step in this direction. (Am. J. Clin. Path., July '47 - Editorial)

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The Use of Music in Industry: A cross-section survey of a number of companies providing music for employees is reported. Of the 111 companies surveyed, 83 provide music during work periods, the others only at lunch, recreation, and other periods. The greater number of employees prefer hit parade music, with swing music next, but classical, semiclassical and other types increase somewhat in popularity after being introduced gradually. A few companies report one or more of the following results: less absenteeism, smaller turnover, decreased accident rates, increase in individual production, better quality of work, less nervous tension, and improvement in punctuality. Fifty-four per cent of the plants report that music promotes greater harmony and good will among workers. About two thirds of the music users are generally satisfied with the music services, and about 9 per cent report dissatisfaction with one or more phases. The sources of music include radio, phonograph records, wired music, and transcription libraries. Each source is used extensively. Many companies encourage employee participation in musical events outside working hours. (Indust. Hyg. Digest., Aug. '47, from Studies in Personnel Policy, No. 78, Nat'l Indust. Conf. Board, 247 Park Ave., New York 17, N. Y. - E. M. Spears)

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Examination for Appointment in Navy Dental Corps: Plans are being formulated to conduct a competitive examination on 3 November 1947 for appointment as lieutenant (junior grade) in the Dental Corps of the U. S. Navy. The examination is scheduled to be given at the following places:

- U. S. Naval Dental School, Bethesda, Maryland
- U. S. Naval Dental Clinic, Brooklyn, New York
- U. S. Naval Station, Norfolk, Virginia
- U. S. Naval Station, Treasure Island, San Francisco, Cal.
- U. S. Naval Training Center, Great Lakes, Illinois
- U. S. Naval Training Center, San Diego, Cal.

Both civilian dentists and dental officers of the Naval Reserve are eligible to apply for this examination provided they are citizens of the United States, between 21 and 32 years of age, and are graduates of acceptable dental colleges. Civilian applicants should submit their applications for permission to appear for the examination to the nearest Office of Naval Officer Procurement. Officers of the Naval Reserve should submit their applications to appear for the examination to the Chief of Naval Personnel via their commanding officer (or Commandant of the Naval District if the applicant is not on active duty) and the Chief of the Bureau of Medicine and Surgery. The attention of Reserve dental officers is invited to ALNAV 591-46 which provides that officers of the Naval Reserve who received their initial commissions after 31 December 1946 are not eligible to transfer to the regular Navy under the current transfer program.

Personnel of the Navy should encourage prospective candidates to apply for permission to take this examination. Such candidates should be informed of that part of Public Law 365 - 80th Congress which provides that officers who are commissioned in the Dental Corps of the regular Navy during the next five years will be entitled to pay at the rate of \$100 per month in addition to the regular pay and allowances. (Dental Div., BuMed)

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(Not Restricted)

Dental Reports and Forms: Copies of dental reports and forms are being received in BuMed in excess of the number desired. This is especially true of the NAVMED-K (Rev. 5-47), REPORT OF DENTAL OPERATIONS AND TREATMENTS. The instructions on this form provide that the original be submitted to BuMed and that an information copy be forwarded to cognizant staff or district dental officers. Copies of forms or reports in excess of those required serve no useful purpose.

Information regarding the number of copies of dental forms and reports which should be made and distributed may be found (1) on the printed form, (2) on page 27, Bumed News Letter of 29 August 1947, or (3) in the Manual of the Medical Department, U. S. Navy. (Dental Div., BuMed)

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(Not Restricted)

New Fourth District Trustee of American Dental Association: Commander Daniel Francis Lynch, DC, USNR, of Washington, D. C., who served on active duty during World War II, was elected the new Fourth District Trustee of the American Dental Association by the House of Delegates at the 88th annual meeting in Boston in August.

As Fourth District Trustee, Commander Lynch will represent the dental sections of the Navy, the Army, the Public Health Service, and the Veterans' Administration; the states of Delaware, Maryland, and New Jersey; the District of Columbia; and Puerto Rico. (Dental Div., BuMed)

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(Not Restricted)

Medical Department Adopts the Standard Nomenclature of Disease and the International Statistical Classification of Diseases, Injuries, and Causes of

Death: As a means of promoting the use of standardized titles for diagnoses, the Bureau of Medicine and Surgery has adopted the Standard Nomenclature of Disease, sponsored by the American Medical Association, as the criterion for diagnostic terms. The Navy nomenclature is now in the process of being revised in order to bring the diagnostic titles into agreement with the Standard Nomenclature. It is also contemplated that the International Statistical Classification of Diseases, Injuries, and Causes of Death, which is now being revised by the World Health Organization, will be adopted by the Navy to serve its statistical purposes. It is anticipated that these two changes will increase the value of naval medical statistics, since the general trend toward standardization both in diagnostic nomenclature and in statistical classification of diseases promises to make the Navy data comparable with medical statistics from an increasing number of governmental and civilian institutions in this country and abroad.

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Opportunities for Active Duty for Naval Reserve Medical Officers: The attention of Reserve medical officers is invited to the opportunities for full-time and part-time active duty

1. Full-Time Duty. Reserve medical officers may return to full-time active duty at one of the major naval air stations of the Naval Air Reserve Training Command or at one of the Naval Air Reserve Training Units (NARTUs), listed below:

NAS Atlanta, Ga.

NAS Columbus, Ohio

NAS Dallas, Texas

NAS Denver, Colo.

NAS Glenview, Ill.

NAS Grosse Ile, Mich.

NAS Los Alamitos, Calif.

NAS Memphis, Tenn.

(Not Restricted)

NAS Miami, Fla.
NAS Minneapolis, Minn.
NAS New York, N. Y.
NAS Oakland, Calif.
NAS Olathe, Kas.
NAS Squantum, Mass.

NAS St. Louis, Mo.
NAS Willow Grove, Pa.
NARTU, NAS Anacostia, D. C.
NARTU, NAS Jacksonville, Fla.
NARTU, NAS Norfolk, Va.
NARTU, NAS Seattle, Wash.

Because The Naval Air Reserve Training Command is increasing in size and activity, consideration is being given to the establishment of several additional stations which will create further openings for inactive Reserve medical officers.

Reserve medical officers who are interested in full-time active duty at one of the stations or units listed above should initiate letters to the Bureau of Naval Personnel, via (1) Chief of Naval Air Reserve Training, Naval Air Station, Glenview, Ill., and (2) Bureau of Medicine and Surgery, Navy Department, Washington, D. C., listing three or four stations, in order of preference, at which duty is desired. Medical officers are desired in the rank of commander and below.

Officers qualifying for the above billets will not be subject to transfer and may terminate their tour of duty at their own request. Flight surgeons are assured of orders to duty involving flying. Officers who have volunteered for active duty in the Naval Air Reserve Training Program may request a course of instruction in Aviation Medicine at the School of Aviation Medicine, Naval Air Station, Pensacola, Fla. This is an eleven weeks' course which leads to the designation of aviation medical examiner. Upon completion of an additional indoctrinational period of duty with an active unit involving actual flying, aviation medical examiners will be designated flight surgeons. Medical officers who have been designated Aviation Medical Examiners or Flight Surgeons are eligible to be given orders to duty involving flying which entitles them to receive the increased flight pay.

In accordance with recent legislation, officers who volunteer for one year or more are entitled to an increase in salary of \$100 per month effective upon the date of reporting for active duty. This is in addition to any other pay and allowances.

Government quarters are available at several of the air stations.

Reserve medical officers awaiting a residency or fellowship in a civilian hospital may wish to consider this opportunity to obtain a full-time paying position while waiting.

2. Part-Time Duty. Naval Reserve flight surgeons who desire to join one of the Navy or Marine combat air groups of the Organized Reserve, training at one of the stations listed above, should contact the local Commanding Officer for additional information. Two months' pay per year is granted for attendance at all training periods. (Personnel Div., BuMed)

(Not Restricted)

Correspondence Pertaining to Army-Navy Catalog of Medical Materiel:

All correspondence pertaining to Army-Navy Catalog of Medical Materiel, other than as directed in ALNAV 185-47 (copy of which appears on page 35 of 12 Sep 1947 Bumed News Letter) should be addressed to:

Bureau of Medicine and Surgery
Materiel Division
84 Sands Street
Brooklyn 1, New York

(Materiel Div., BuMed)

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(Not Restricted)

Change in "Reports from Dental Departments": The 29 August 1947 issue of Bumed News Letter contained, on page 27, a notice, "Reports from Dental Departments" in which there was a table headed "Principal Reports Required from Dental Departments Ashore and Afloat." The asterisks in the third column of that table signified that a copy of the report so marked was to be sent to the cognizant staff or district dental officer. The asterisk for NAVMED-L should be deleted. (Dental Div., BuMed)

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(Not Restricted)

Part I of the Examination of the American Board of Orthopedic Surgery:

The Bureau of Medicine and Surgery has been informed that applications for Part I of the examination of The American Board of Orthopedic Surgery must be received by the Secretary, Dr. Francis M. McKeever, 1136 West 6th Street, Los Angeles 14, California, NOT LATER THAN 15 January 1948. Early compliance should be made by those who contemplate taking this examination.

Information relative to examining centers and dates will be announced at a later date. (Professional Div., BuMed)

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(Not Restricted)

Public Health Foreign Reports:

<u>Disease</u>	<u>Location</u>	<u>Date</u>	<u>No. of Cases</u>
Cholera	India, Calcutta	June 8-14, '47	263 (63 fatal)
		June 22-28, '47	152 (43 fatal)
	Lukenow	June 29-July 5, '47	120 (21 fatal)
	Siam (Thailand)	June 1-7, '47	75 (54 fatal)
		June 29-July 5, '47	245 (166 fatal)
Plague	Brazil	January 1947	7 (2 fatal)
		February 1947	2 (fatal)

(Not Restricted)

Public Health Foreign Reports (Cont.):

<u>Disease</u>	<u>Location</u>	<u>Date</u>	<u>No. of Cases</u>
Plague (bubonic)	China, Chekiang Prov., Wenchow	May 11-20, '47	11
	Fukien Prov., Amoy	June 1-11, '47	5
	Ecuador, Loja Prov., Loja Canton, Trapichillo	June 1-7, '47	3
	Egypt, Alexandria	July 12-19, '47	3
	Germany (Russian Zone), East Prussia, Koenigsberg	June 1947	unknown (mor- tality rate seri- ous)
	Indochina (French) Cochinchina, Cholon	May 21-31, '47	1
	Korea	April 1947	22
	Peru	May 1947	6 (3 fatal)
	(pneumonic) Union of S. Africa, Transvaal, Johannesburg	July 19, '47	2
	Smallpox Angola	January 1947	13
(8 suspected)	Colombia	May 1947	813 (13 fatal)
		June 1947	533 (1 fatal)
	Ecuador	June 1947	61 (1 fatal)
	Egypt, Port Said	June 29-July 5, '47	1
	Great Britain, England	June 15-21, '47	10
		June 29-July 12, '47	5
	Iraq, Basra	June 1-7, '47	4
	Ivory Coast	June 21-30, '47	311
	Mexico, Toluca	June 22-28, '47	55
	Rhodesia, Southern	April 1947	118 (21 fatal)
Typhus Fever	Colombia	May 1947	238 (4 fatal)
		June 1947	228 (5 fatal)
	Rumania	May 21-June 7, '47	1,710
		June 16-21, '47	726
	Tunisia	May 1947	129
		June 21-30, '47	71
Yellow Fever	Colombia, Boyaca Dept.	May 21, '47	1 (fatal)

(Not Restricted)

Public Health Foreign Reports (Cont.):

<u>Disease</u>	<u>Location</u>	<u>Date</u>	<u>No. of Cases</u>
Yellow Fever	Colombia		
	Intendencia of Meta	May 26, '47	1 (fatal)
		May 28, '47	1 (fatal)
		June 19, '47	2 (fatal)
	Santander Dept.	May 10-13, '47	1 (fatal)
		June 1-15, '47	1 (fatal)
	Tolima Dept.	June 9, '47	1 (fatal)
	Gold Coast, Western		
(suspected)	Prov., Bogosu	June 24, '47	1 (fatal)

(Pub. Health Reps., 19 July; 1, 8, 15, and 29 Aug.; and 5 Sept. '47)

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Circular Letter 47-120

5 September 1947

(Not Restricted)

To: All Ships and Stations

Subj: Roentgenographic Examinations of the Chests of Navy and Marine Corps Personnel; Forms for Recording and Reporting of,

Ref: (a) Par. 21103, Manual of the Medical Department.

1. Reference (a) has been revised and is in the process of being printed and distributed as part of printed page change 2 of the Manual. This revised paragraph provides for the use of the following forms for the recording and reporting of roentgenographic examinations of the chest:

<u>Form</u>	<u>Title</u>	<u>No. sheets to a pad</u>
NAVMED-618 (Rev. 3-47)	Report of Photofluorographic Chest Survey	25
NAVMED-1161 (2-47)	Photofluorographic Log	25
NAVMED-1161(a) (2-47)	Following Sheet	100

2. The above mentioned forms are being stocked at the District Publications and Printing Offices and requiring activities shall address their requests thereto. Stocks are to be limited to a three months' supply.

--BuMed. C. A. Swanson

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Circular Letter 47-121

8 September 1947

(Not Restricted)

To: All Ships and Stations

Subj: Drugs, Narcotics, Alcohols, Blood Derivatives, and Special Control Items; Disposition of,

Refs: (a) NPR&DR #1, Change #5, May, 1947
 (b) NPR&DR #3, March, 1946
 (c) NPR&DR #4, Revision #1, February, 1946

1. Attention is directed to refs (a), (b), and (c), as may be applicable to geographic location of addressees, for strict compliance in connection with disposition of the subject items. Specifically, attention is invited to instructions regarding disposition of those selected items listed in par. 606.6, ref (a), and in BuMed Control Lists in refs (b) and (c). All consuming activities, ashore and afloat, are hereby expressly forbidden to declare as surplus any BuMed controlled item included in the above references. If any such item is included, either as loose stock or as a component of a self-contained unit, in the inventory of property which is to be declared surplus or of a ship which is to be sold, such

(Not Restricted)

item will be removed therefrom and disposed of as directed by refs (a), (b), or (c), depending on physical location of the disposing activity.

2. The above directions do not in any way modify existing instructions regarding transfer of BuMed excess property between naval activities.

--BuMed. H. L. Pugh

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Circular Letter 47-122

9 September 1947

(Not Restricted)

To: All Senior Medical Officers.

Subj: Training in Aviation Medicine.

1. It is requested that this letter be brought to the attention of every medical officer under your cognizance.

2. The Bureau of Medicine and Surgery announces the next class in Aviation Medicine will convene at the U. S. Naval School of Aviation Medicine, Pensacola, Florida on 5 January 1948, for a quota of 40 students. Duration of course is 3 months and no service agreement is required.

3. Eligibility requirements are:

(a) Rank of Lt. (jg), Lieut. and Lt. Comdr.

(b) Reserve medical officers may apply who will have 15 months obligated service after completion of the course.

(c) Reserve medical officers who have less than 15 months obligated service may apply, providing they request transfer to the regular Navy at the same time the request for Aviation Medicine is submitted.

4. Applications are desired to reach BuMed prior to 15 November 1947 and may be made by dispatch. Aviation Medicine training provides basis for later assignment in Aviation Medical Research or other specialties in the Training Program.

--BuMed. H. L. Pugh

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Circular Letter 47-123 (Not released in time for inclusion in this issue.)

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Circular Letter 47-124

12 September 1947

(Not Restricted)

To: All Ships and Stations

Subj: NAVMED-N, Certificate of Death; Preparation of

Refs: (a) ALNAV 566, dtd 17 Oct 1946

(b) Manual of the Medical Department, U. S. Navy, Change 1,
Pars. 344 and 348.

1. Relative to submission of NAVMED-N, Certificate of Death, ref. (a) was superseded by ref. (b) on 1 January 1947.
2. In order to clarify the manner of recording the information required by ref. (b), it is directed that appropriate notation as to "active, inactive or training duty status" be entered under the space for RANK OR RATE; furthermore, LENGTH OF SERVICE shall be reported for active duty personnel only and on the same line for NATIONALITY in the space just preceding RELIGION.
3. Instructions for reporting PLACE OF ORIGINAL ADMISSION are adequate on the NAVMED-N and this information need be recorded for only active duty personnel. This item shall be reported as the ship or station to which the decedent was attached when first admitted to the sick list, that is, the patient's last active duty station prior to the period on the sick list which terminated in death.

--BuMed. C. A. Swanson

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Circular Letter 47-125

12 September 1947

(Not Restricted)

To: All Ships and Stations

Subj: Medicinal Gases, Identification of

Ref: (a) BuMed Circular Letter 47-73 of 12 June 1947

1. Reference (a) established the policy whereby all medicinal gases employed in the treatment of patients will be obtained from supply facilities under the cognizance of BuSanda. It is probable that the color identification of gas cylinders will be revised as a result of studies recently conducted by Federal agencies. Accordingly, the attention of all Medical Department personnel is called to the necessity of proper identification of medicinal gases prior to use. Gas cylinders are identified by two means, i.e., a color code and a label.
2. All Medical Department personnel employing medicinal gases shall positively identify gases employed by means of the label attached. The color code may be

(Not Restricted)
used as an aid in stowage and handling only, but shall never be relied upon for the purpose of identifying the medicinal substance contained in the cylinder at time of administration.

--BuMed. H. L. Pugh

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Circular Letter 47-126 12 September 1947 (Not Restricted)

To: All Ships and Stations

Subj: NavMed Forms, Stocks of

Ref: (a) BuMed Circular Letter 46-101, Item 46-1381, Navy Department Bulletin

1. Reference (a) is hereby canceled.

2. District Publications and Printing Offices have been established in all naval districts, with the exception of the tenth, and NavMed forms are stocked therein. District activities shall submit requests for NavMed forms to their respective DP&PO. Tenth Naval District, non-district, and fleet activities shall submit their requests to the most conveniently located DP&PO.

--BuMed. H. L. Pugh

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Circular Letter 47-127 12 September 1947 (Not Restricted)

To: All Activities Having Photofluorographic Units Equipped with Navy Automatic Camera, Stock No. 6-008-025.

Subj: Camera, Photoroentgen and Radiographic Unit, 35 mm., 50 Ft. Film, 110 Volt, 60 Cycle, A. C., Stock No. 6-008-025, Excess Camera Units and Parts, Request for Transfer of,

This letter from the Deputy and Assistant Chief of BuMed requests that addressees determine the quantity on hand of the following items and transfer all in excess of one each to the U. S. Naval Hospital, National Naval Medical Center, Bethesda, Maryland, for disposition:

- (a) Navy automatic 35 mm. camera (Stock No. 6-008-025).
- (b) Control box for Navy automatic camera (Stock No. NS-6).
- (c) Connecting cables for Navy automatic camera (Stock No. NS-6).
- (d) Mounting plates for Navy automatic camera (Stock No. NS-6).
- (e) Leica Fl.5 lens (Stock No. NS-6).

Circular Letter 47-128

16 September 1947

(Not Restricted)

To: All Ships and Stations

Subj: Annual Physical Examinations - Calendar Year 1947.

Ref: (a) General Order 191 of 28 May 1943.

1. The following is promulgated for guidance in connection with the annual physical examination required by ref (a):

- (a) Physical examinations conducted during the calendar year 1947 in the cases of officers of the Naval Reserve or temporary officers USN for the purpose of determining physical fitness for permanent appointment in the regular Navy will obviate the necessity of conducting an annual physical examination in such cases.
- (b) A physical examination conducted incident to temporary promotion shall be considered as not sufficient to obviate the necessity of an annual physical examination.
- (c) Attention is invited to the provisions of paragraph 21104, Manual of the Medical Department, in connection with the conduction of the annual physical examination. In evaluating fitness for duty due consideration shall be given action taken on recent reports by Boards of Medical Survey and also to existing waiver of defect or disease.
- (d) An electrocardiogram shall be conducted in the cases of all officers who are 45 years of age or over. A complete blood count and sedimentation index, a blood Kahn test, a prostatic examination, or any other special study that may be indicated shall be performed at the discretion of the examiner.
- (e) In those cases where a chest X-ray study has not been conducted within the past year as required by paragraph 21103.2, Manual of the Medical Department, a chest X-ray study shall be conducted as a part of the annual physical examination.
- (f) There will be no special boards convened for the purposes of examining senior officers.

2. Attention is invited to existing instructions which require that a NAVMED-Y or a NAVMED-AV-1 in the case of aviators, be completed and forwarded only in those cases in which defects are discovered which are regarded as sufficient to impair the examinee's ability to perform his duties. When such reports are forwarded the examiner shall indicate the proposed local action to be taken,

(Not Restricted)

whether it be observation on active duty; ambulatory treatment; transfer to hospital at once or when later indicated; professional advice intended for correction, arrest, or improvement in disease process; or other appropriate action. Indiscriminate transfer to a hospital should be avoided, but such disposition may be warranted early in the course of a disease such as arterial hypertension to afford thorough case study and fully considered corrective and preventive therapeutic program. In those cases wherein officers are physically qualified in all respects, an entry on NAVMED-H-8 of the Health Record constitutes an appropriate record of the examination.

3. Attention is invited to the provisions of paragraphs 21104 and 2221.4, Manual of the Medical Department, regarding the forwarding of reports of annual physical examinations. The letter of transmittal required in paragraph 5 of ref (a) shall be omitted.

--BuMed. H. L. Pugh

--BuPers. T. L. Sprague

--MarCorps. A. A. Vandegrift

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Circular Letter 47-129

16 September 1947

(Not Restricted)

To: All Naval Hospitals, Continental U.S.

Subj: NAVMED I (Report of Patients); Forwarding of

Ref: (a) Manual of the Medical Department, Par. 5111

1. It is directed that steps be taken to expedite the forwarding to the Bureau of NAVMED I (Report of Patients). As indicated in reference (a), the reports are to be forwarded direct to the Bureau not later than Friday of each week. Activities west of the Mississippi shall forward their reports by air mail.

2. These reports constitute the bases of many analyses essential to the various divisions of the Bureau, so that delay in receipt of the reports impairs their usefulness and reflects detrimentally in the summary.

--BuMed. H. L. Pugh

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ALNAV 196

8 September 1947

(Not Restricted)

Subj: Running Mates of Medical Corps Junior Grade Lieutenants Appointed Subsequent to 7 August 1947.

Refer Alnav 184. Public Law 381 - 80th Congress provides that lieutenants junior grade Medical Corps appointed subsequent to 7 August 1947 pursuant any authority other than Public Law 347 - 79th Congress be assigned running mates with date of rank in preceding calendar year. Therefore those lieutenants junior grade USNR who completed internship subsequent to 31 December 1946 and who desire to transfer to regular Navy should give consideration to advantages accruing due to earlier date of rank of those who are successful in professional examinations leading to direct appointment. Information on next professional examinations to be given 6 October 1947 available at all naval hospitals and offices of district medical officers. Applications of officers on active duty may be submitted in form of letter request for authority to participate accompanied by recommendation of commanding officer. Letter should be addressed Chief of Naval Personnel, Attention Pers 3639, via BuMed Code 3424.

--SecNav.

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(For returning this questionnaire there is enclosed an envelope requiring no postage and addressed to the Division of Medical Statistics, Bureau of Medicine and Surgery, Navy Department, Potomac Annex, Washington 25, D. C.)

QUESTIONNAIRE ON BUMED NEWS LETTER

The Bureau of Medicine and Surgery has received many comments on the Bumed News Letter. It is realized, however, that in view of the large distribution of the Bumed News Letter, these appraisals are not necessarily representative of the general attitude. For that reason and in order to obtain a basis upon which to determine whether the Bumed News Letter is to be continued as it is at present, issued less often, or deleted, it is essential to obtain from as many of its recipients as possible an unbiased and critical evaluation of its worth and usefulness to them. For this purpose please check your answers to the following questions:

1. Do you receive the Bumed News Letter:

regularly —
irregularly —
occasionally —

2. Do you read the Bumed News Letter as received:

all issues —
most issues —
occasional issues —
rare issues —

3. What section or sections do you read:

professional —
notices —
circular letters —

4. Do you consider the professional material in the Bumed News Letter to be of:

great value —
moderate value —
little value —
no value —
no opinion —

5. Do you consider the notices in the Bumed News Letter to be:

very useful —
moderately useful —
slightly useful —
of no value —

6. Do you consider inclusion of the circular letters to be:

essential —
highly desirable —
sometimes useful —
of no value —

7. Do you believe it most useful for the Letter to be issued:

weekly —
biweekly (as at present) —
monthly —
not at all —
no opinion —

8. Do you consider that the amount of professional material contained is:

sufficient —
too little —
too much —
no opinion —

9. In your own field is the professional material of:

particular interest —
some interest —
little interest —
no interest —

10. In clarity, conciseness, and readability, do you consider the professional material to be:

very well presented —
well presented —
fairly well presented —
poorly presented —
no opinion —

11. Would you like the size of printing to:

remain the same —
be made smaller —
be made larger —
no preference —

12. Would material in smaller print in two columns per page be:

more desirable —
less desirable —
acceptable —
unacceptable —
no opinion —

The information desired below would be very useful but is not essential in this study. Please fill in as many of the spaces below as you see fit.

Rate: _____ Rank: _____

Regular USN: _____ Active Reserve: _____ Inactive Reserve: _____

Specialty, if any: _____

Present Job: _____

Name: _____

Any additional comments are invited: